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(54) Titl
USE OF PARTIAL OR COMPLETE EXTRACT OF NOT FERMENTED CAMELLIA SINENSIS L. FOR THE PREPARATION OF A MEDICAMENT, A MEDICAL CARE PRODUCT, A COSMETIC PREPARATION OR A FOOD COMPLEMENTARY PRODUCT

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(57) Claim

1. Use of a partial or complete extract of not fermented Camellia sinensis L. for the preparation of a medicament, a medical care product, a cosmetic preparation or a food complementary product, whereby these preparations

- prevent or at least reduce considerably the formation of necrosis and/or atrophies in human or animal tissues and/or the premature mortification of vascularized and non-vascularized cells and cellular tissues/colonies in the human or animal body, and

- not only promote the adhesion between single, to the same tissue type belonging cells or cell unions,

- but also prevent or at least reduce considerably the adhesion between single, to different not histo-compatible tissue types belonging cells or cell unions.

9. Use according to one of claims 1 to 8, characterized in that said preparations serve for the treatment of human or animal cell and/or tissue cultures as well as organs outside the human or animal body, especially for the cultivation and propagation and/or the three-dimensional reconstruction of cartilage cells, gingiva cells, hair root cells, skin cells and skin tissues, retina cells and retina tissues, heart muscle cells and heart muscle tissues, liver cells and liver tissues.

10. A method for the treatment of the human or animal body, characterized in that a medicament, a medical care product or a food complementary product is administered to the human or animal body, whereby these preparations comprise a partial or complete extract of not fermented Camellia sinensis L., and whereby these preparations

- prevent or at least reduce considerably the formation of necrosis and/or atrophies in human or animal tissues and/or the premature mortification of vascularized and non-vascularized cells and cellular tissues/colonies in the human or animal body, and

- not only promote the adhesion between single, to the same tissue type belonging cells or cell unions,

- but also prevent or at least reduce considerably the adhesion between single, to different not histo-compatible tissue types belonging cells or cell unions.

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COMPLETE SPECIFICATION

NAME OF APPLICANT(S):

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INVENTION TITLE:

Use of a partial or complete extract of not fermented Camellia sinensis L. for the preparation of a medicament, a medical care product, a cosmetic preparation or a food complementary product

The following statement is a full description of this invention, including the best method of performing it known to me/us:–

The present invention is directed to the use of a partial or complete extract of not fermented Camellia sinensis L. for the preparation of a medicament, a medical care product, a cosmetic preparation or a food complementary product.

Preparations of Camellia sinensis L. for medical and cosmetic applications are known; see "Hagers Handbuch der Pharmazeutischen Praxis", Vol. 4, Drogen A-D, Springer-Verlag, (1992), pages 628 - 640.

Due to its content compounds Camellia sinensis L. has a central stimulating, moderate diuretic, in dependence of the extraction time more or less strong constipatory/anti-diarrhoeal, the heart activity promoting and possibly antiarteriosclerotic effect, see Stagg G.V., Millin D.J., (1975), J. Sci. Food. Agric. 26, pages 1439 - 1459.

The further prior art concerning Camellia sinensis L. is described in Zeitschrift für Phytotherapie 17, (1995), pages 231 - 250.

So are especially assigned to the in Camellia sinensis L. contained polyphenols an antioxidant efficacy, which shall protect the human body from so called radicals.

The polyphenols are also assigned to have an anti-inflammatory efficacy.

An inhibition of the tumor formation by means of Camellia sinensis L. extracts has been proved in animal experiments and is supported by epidemiological studies.

Also mentioned are virostatic and bacteriostatic effects of Camellia sinensis L. extracts.

In JP 07/101 837 is described an agent having anti-dandruff activity. As active component this agent contains an alcoholic extract of not further specified tea leaves.

In JP 06/056 687 is described an agent with which is removed dental tartar, and with which the formation of dental tartar is prevented.

As active components this agent contains an aqueous or a with a hydrophilic organic solvent obtained extract of tea leaves (Camellia sinensis).

For the claimed activity has been made responsible the strong antimicrobial effect against periodontotic pathogenic bacterias.

In JP 08/073 350 is described an agent for the improvement of cerebral functions.

As active component is mentioned theanine (glutamic acid ethylamide). This component may be contained in tea extracts.

In JP 06/100 442 is described an anti-stress agent for the prevention or mitigation of mental and physical diseases due to stress.

As active component this agent contains L-theanine of native origin as such or in the form of a pharmaceutically acceptable salt, for example the hydrochloride.

In US 5 071 653 are described processes for the preparation of extracts of Camellia sinensis.

These extracts promote the growth of bifidobacterias.

These extracts contain in contrary to tea infusions, partial and complete extracts of not fermented Camellia sinensis neither flavone glucosides nor polyphenols, and also no therpenoides and no lipophilic compounds.

With these in US 5 071 653 described processes are made highly selective fractionations of Camellia sinensis content compounds, which have a completely unusual activity spectra, that is the promotion of the growth of intestine bacterias.

Quite surprisingly were found new use possibilities of partial or complete extracts of not fermented Camelia sinensis L.

The present invention is directed to the use of a partial or complete extract of not fermented Camellia sinensis L. for the preparation of a medicament, a medical care product, a cosmetic preparation or a food complementary product, whereby these preparations

- prevent or at least reduce considerably the formation of necrosis and/or atrophies in human or ani-

mal tissues and/or the premature mortification of vascularized and non-vascularized cells and cellular tissues/colonies in the human or animal body, and

- not only promote the adhesion between single, to the same tissue type belonging cells or cell unions,

- but also prevent or at least reduce considerably the adhesion between single, to different not histo-compatible tissue types belonging cells or cell unions.

Preferred embodiments of this invention are defined in the dependent claims.

The extract of Camellia sinensis L. used for the examinations described below was prepared as follows.

6 kg dried, not fermented Camellia sinensis L. (folia) were extracted under stirring with 60 kg of a mixture of 8 parts by weight of ethanol and 2 parts by weight of water at a temperature from 25°C to 35°C during 2 hours.

Then was filtered, and the solvent mixture was evaporated at a pressure from 50 mbar to 150 mbar and a temperature from 30°C to 40°C up to a complete evaporation of ethanol.

From the so obtained concentrate were removed according to EP 0 730 830 A1 the undesired lipophilic contaminations and residues.

The so purified extract was then subjected to a process for a decrease of the bacterial count (30 seconds at a temperature of 120°C).

Then this extract was spray dried.

There was obtained 1 kg of native dry extract having the following analysis datas.

50 % m/m phenylchroman derivatives, calculated as epicatechin (HPLC),

6 % m/m caffeine (HPLC)

1 % m/m theobromine (HPLC).

In addition were detected qualitatively:

glutaminic acid-ethylamide

flavonoides and

plant acids (HPTLC).

This product is obtainable from the company Emil Flachsmann AG in CH-8820 Wädenswil / Switzerland under the denotation "EFLA 85942".

This product was tested on its effects on a special cell model, that is the multicellular spheroids.

These spheroids are ball-shaped cell aggregates, which contain in suspension culture at a diameter of about 1 mm up to 100'000 cells, and as a rule reflect

better the biological relations of cell unions in vivo than conventional monolayer cultures.

Experiment 1

Tested was the influence of the product "EFLA 85942" onto the volume growth of these spheroids as a function of the cultivation length and at different concentrations of "EFLA 85942" in comparision to control cultures.

The following results were obtained.

As expected "EFLA 85942" effected a systematic and in large ranges of the growth length a significant reduction of the volume growth of the spheroids.

But quite surprisingly no concentration dependence could be detected thereby after the beginning of the effect over a broad concentration range.

This effect points to a high therapeutical width.

In addition it was noted quite surprisingly that the with "EFLA 85942" treated spheroides formed no noteworthy necrosis during the whole growth phase.

In control cultures which were not treated with "EFLA 85942" already at diameters of about 200 micrometers were detected central necrosis which increased strongly during the growth phase.

At the end of the duration of test the untreated spheroids showed only a very thin vital border layer.

This occurance of necrosis is typical for the used experimental model.

This behaviour of the with "EFLA 85942" treated spheroids has not yet been observed.

It is persumed that the known antioxidative effect of the polyphenols can not be responsible alone for this behaviour.

On behalf of this may be used also the results which were obtained from accompanying investigations on singly cells; see experiment 2.

Experiment 2

In a first experiment were sowed colon carcinoma cells under the influence of "EFLA 85942" in so called adhered culture flasks.

Expected was the formation of a so called monolayer-film.

But quite surprisingly was observed the formation of three-dimensional, strongly connected cell aggregates.

Also this behaviour has not yet been observed.

In addition were observed in the culture media nearly no non-adhered single cells.

In a second experiment some few single cells were sowed in non-adhered Petri dishes, with the aim to analyze the influence of "EFLA 85942" onto the colony generation ability of these single cells.

Thereby two variants were carried out.

In experiment A was added "EFLA 85942" to the cells after an initial adhesion on the Petri dish.

In experiment B was added "EFLA 85942" to the cells immediately before the adhesion process.

In these two experiments could be determined a statistical significant decrease of the colony generation ability which occured in experiment B, in comparision to experiment A, in a drastic stronger extent.

The result of these two experiments, together with the above described formation of three-dimensional cell aggregates, allows the conclusion that on one hand the adhesion with non histo-compatible structures is reduced and that on the other hand the adhesion betweeen single, to the same tissue type belonging cells or cell unions is promoted.

These behaviour characteristics prove that beside the above mentioned antioxidative effect of the polyphenols still further effect mechanisms and/or further active compounds play an important rule.

The treatment of the human or animal body may consist therein that the corresponding preparation is taken or is applied internal or external.

The treatment is carried out at least during such a long time until the corresponding symptomatic has disappeared.

The following examples illustrate the present invention.

Example 1

Preparing of a preparation in the form of a hard gelatin capsule.

For the preparation of 1000 capsules of the size "one " 100 g of "EFLA 85942" were mixed homogeneously with 25 g of microcristalline cellulose, 4 g of magnesium stearate and 1 g of precipitated silicic acid.

This mixture was filled in a respective amount of 150 mg into hard gelatin capsules.

Example 2

Preparing of a preparation in the form of a drinking ampule.

For the preparation of 1000 drinking ampuls of 10 ml 100 g of "EFLA 85942" were mixed homogeneously with 15 g of potassium sorbate, 15 g of sodium benzoate, 500 g of fructose and 10 g of sodium chloride.

This mixture was filled up with a solution of 95 parts by weight of water and 5 parts by weight of glycerol to a total volume of 10 liters, mixed and filtered sterile.

The obtained filtrate was filled aseptic into the drinking ampules.

Example 3

Preparing of a preparation in the form of a liposome gel.

Phase A

- 1.0 parts by weight of Rhodigel[R] 200,

- 8.0 parts by weight of 1,2-propylene glycol

were mixed at room temperature and were allowed to swell during one hour.

Phase B

- 6.5 parts by weight Phospholipon[R] 80,

- 10.0 parts by weight of polyethylene glycol 400,

- 2.0 parts by weight of glycerol

were mixed together at a temperature from 60°C to 70°C and were homogenized.

The obtained homogeneous mixture was cooled to a temperature from 38°C to 40°C under stirring.

Phase C

A mixture of

- 71.7 parts by weight of distilled water,

- 1.2 parts by weight of "EFLA 85942"

was filtered sterile and was then incorporated drop by drop into the phase B. After the complete addition the obtained mixture was cooled to room temperature, incorporated in portions into the phase A and homogenized.

The obtained preparation can be filled in plastic squezze bottles of 10 ml.

The preparation was prepared unter aseptic conditions.

Application example 1

A 30 years old female healthy test person with head hair problems in the form of thin areas and partially growed places took over a time of 8 weeks daily 3 capsules according to example 1.

Within this time the state of the head hair changed drastically.

In the growed hair areas germinated normally coloured hairs, and the thin areas disappeared.

Application example 2

A 36 years old male healthy test person with head hair problems in the form of thin areas and partially growed places took over a time of 8 weeks daily 6 capsules according to example 1.

Within this time the state of the head hair changed drastically.

In the growed hair areas germinated normally coloured hairs, and the thin areas disappeared.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. Use of a partial or complete extract of not fermented Camellia sinensis L. for the preparation of a medicament, a medical care product, a cosmetic preparation or a food complementary product, whereby these preparations

- prevent or at least reduce considerably the formation of necrosis and/or atrophies in human or animal tissues and/or the premature mortification of vascularized and non-vascularized cells and cellular tissues/colonies in the human or animal body, and

- not only promote the adhesion between single, to the same tissue type belonging cells or cell unions,

- but also prevent or at least reduce considerably the adhesion between single, to different not histo-compatible tissue types belonging cells or cell unions.

2. Use according to claim 1, characterized in that the medicament or the medical care product is in a pharmaceutically acceptable administrative form, especially in

- solid administrative forms for oral application, especially in the form of a tablet, a filmtablet, a dragee, a pellet, a hard gelatin-capsule, a soft gelatin-capsule,

- liquid administrative forms for oral, parenteral, rectal, vaginal and topic application, especially

in the form of a dropping solution, a spray, an injection solution, a syrup,

- semisolid administrative forms for topic, oral, rectal and vaginal application, especially in the form of a cream, a gel, an ointment, a paste, a suppository.

3. Use according to claim 1, characterized in that the cosmetic preparation or the food complementary product is in the form of a solution, a spray, a cream, a gel, an ointment, a paste, a dragee, a capsule, an ampule or a shampoo.

4. Use according to one of claims 1 to 3, characterized in that the partial or complete extract is incorporated into nano-capsules or into liposomes.

5. Use according to one of claims 1 to 4, characterized in that said preparations contain additionally at least one additive and/or auxiliary agent, especially selected from the group, consisting of emulsifiers, stabilizers, antioxidants, dyestuffs, aromas, disintegration agents, solvents, lubricants and surfactants.

6. Use according to one of claims 1 to 5, characterized in that the partial or complete extract is contained in an amount from 0.1 % by weight to 95 % by weight, referred to the total weight of the preparation.

7. Use according to one of claims 1 to 6, characterized in that the partial or complete extract contains besides native, polyphenols and purine alkaloids additionally at least one further native compound, se-

lected from the group consisting of glutamic acid ethylamide, glutamic acid, including their physiologically salts, and glutamine.

8. Use according to one of claims 1 to 7 characterized in that said preparations serve for the prevention, treatment or post-treatment of

- cachectic states, be affected by small intestine villus atrophies,

- malabsorptions, be affected by small intestine villus atrophies,

- polyneuropathias, be affected by non-inflammatory axon damages,

- parodontosis, be affected by gingiva cell growth disorders and cell-cell-adhesion disorders,

- loss of hair, be affected by hair root atrophies,

- hypertrophic skin changes, for example psoriasis vulgaris, neurodermitis, be affected by cell-cell-adhesion disorders and lacks of differentiation,

- hyperplasias, be affected by pathological cell propagation, for example hypersplenism, be affected by lymphogranulomatosis, foveolic hyperplasia of the gastric mucosa,

- leukozytes-maturation disorders, for example leukaemias of the subspecies

a.) acute lymphatic leukaemia,

b.) chronic lymphatic leukaemia,

c.) acute myeloic leukaemia, especially of the peroxidase-type,

d.) chronic myeloic leukaemia,

- exsudative forms of the tuberculosis of the lungs,

- zirrhosis of the lungs, for example chronic interstitial fibrosis with parenchyma depletion,

- zirrhosis of the liver, for example as a consequence of chronic hepatitis,

- emphysemas of the lungs, or

- erythematodes visceralis.

9. Use according to one of claims 1 to 8, characterized in that said preparations serve for the treatment of human or animal cell and/or tissue cultures as well as organs outside the human or animal body, especially for the cultivation and propagation and/or the three-dimensional reconstruction of cartilage cells, gingiva cells, hair root cells, skin cells and skin tissues, retina cells and retina tissues, heart muscle cells and heart muscle tissues, liver cells and liver tissues.

10. A method for the treatment of the human or animal body, characterized in that a medicament, a medical care product or a food complementary product is administered to the human or animal body, whereby these preparations comprise a partial or complete extract of not fermented Camellia sinensis L., and whereby these preparations

- prevent or at least reduce considerably the formation of necrosis and/or atrophies in human or animal tissues and/or the premature mortification of vascularized and non-vascularized cells and cellular tissues/colonies in the human or animal body, and

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- not only promote the adhesion between single, to the same tissue type belonging cells or cell unions,

- but also prevent or at least reduce considerably the adhesion between single, to different not histo-compatible tissue types belonging cells or cell unions.

11. the method according to claim 10, characterized in that the medicament or the medical care product is in a pharmaceutically acceptable administrative form, especially in

- solid administrative forms for oral application, especially in the form of a tablet, a filmtablet, a dragee, a pellet, a hard gelatin-capsule, a soft gelatin-capsule,

- liquid administrative forms for oral, parenteral, rectal, vaginal and topic application, especially in the form of a dropping solution, a spray, an injection solution, a syrup,

- semisolid administrative forms for topic, oral, rectal and vaginal application, especially in the form of a cream, a gel, an ointment, a paste, a suppository.

12. The method according to claim 10, characterized in that the food complementary product is in the form of a solution, a spray, a cream, a gel, an ointment, a paste, a dragee, a capsule, an ampule or a shampoo.

13. The method according to one of claims 10 to 12, characterized in that the partial or complete extract is incorporated into nano-capsules or into liposomes.

14. The method according to one of claims 10 to 13, characterized in that said preparations contain additionally at least one additive and/or auxiliary agent, especially selected from the group, consisting of emulsifiers, stabilizers, antioxidants, dyestuffs, aromas, disintegration agents, solvents, lubricants and surfactants.

15. The method according to one of claims 10 to 14, characterized in that the partial or complete extract is contained in an amount from 0.1 % by weight to 95 % by weight, referred to the total weight of the preparation.

16. The method according to one of claims 10 to 15, characterized in that the partial or complete extract contains besides native, polyphenols and purine alkaloids additionally at least one further native compound, selected from the group consisting of glutamic acid ethyl-amide, glutamic acid, including their physiologically salts, and glutamine.

17. The method according to one of claims 10 to 16 characterized in that said preparations serve for the prevention, treatment or post-treatment of

- cachectic states, be affected by small intestine villus atrophies,

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- malabsorptions, be affected by small intestine villus atrophies,

- polyneuropathias, be affected by non-inflammatory axon damages,

- parodontosis, be affected by gingiva cell growth disorders and cell-cell-adhesion disorders,

- loss of hair, be affected by hair root atrophies,

- hypertrophic skin changes, for example psoriasis vulgaris, neurodermitis, be affected by cell-cell-adhesion disorders and lacks of differentiation,

- hyperplasias, be affected by pathological cell propagation, for example hypersplenism, be affected by lymphogranulomatosis, foveolic hyperplasia of the gastric mucosa,

- leukozytes-maturation disorders, for example leukaemias of the subspecies

a.) acute lymphatic leukaemia,

b.) chronic lymphatic leukaemia,

c.) acute myeloic leukaemia, especially of the peroxidase-type,

d.) chronic myeloic leukaemia,

- exsudative forms of the tuberculosis of the lungs,

- zirrhosis of the lungs, for example chronic interstitial fibrosis with parenchyma depletion,

- zirrhosis of the liver, for example as a consequence of chronic hepatitis,

- emphysemas of the lungs, or

- erythematodes visceralis.

18. The method according to one of claims 10 to 17, characterized in that said preparations serve for the treatment of human or animal cell and/or tissue cultures as well as organs outside the human or animal body, especially for the cultivation and propagation and/or the three-dimensional reconstruction of cartilage cells, gingiva cells, hair root cells, skin cells and skin tissues, retina cells and retina tissues, heart muscle cells and heart muscle tissues, liver cells and liver tissues.

19. The steps, features, compositions and compounds disclosed herein or referred to or indicated in the specification and/or claims of this application, individually or collectively, and any and all combinations of any two or more of said steps or features.

DATED this TWENTY FOURTH day of OCTOBER 1997

Emil Flachsmann AG

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Patent Attorneys for the applicant(s)

Abstract

The present invention is directed to the use of a partial or complete extract of not fermented Camellia sinensis L. for the preparation of a medicament, a medical care product, a cosmetic preparation or a food complementary product, whereby these preparations

- prevent or at least reduce considerably the formation of necrosis and/or atrophies in human or animal tissues and/or the premature mortification of vascularized and non-vascularized cells and cellular tissues/colonies in the human or animal body, and

- not only promote the adhesion between single, to the same tissue type belonging cells or cell unions,

- but also prevent or at least reduce considerably the adhesion between single, to different not histo-compatible tissue types belonging cells or cell unions.